

Systemic lupus erythematosus: features

Systemic lupus erythematosus (SLE) is a multisystem, autoimmune disorder. It typically presents in early adulthood and is more common in women and people of Afro-Caribbean origin.

General features

- fatigue
- fever
- mouth ulcers
- lymphadenopathy

Skin

- malar (butterfly) rash: spares nasolabial folds
- discoid rash: scaly, erythematous, well demarcated rash in sun-exposed areas. Lesions may progress to become pigmented and hyperkeratotic before becoming atrophic
- photosensitivity
- Raynaud's phenomenon
- livedo reticularis
- non-scarring alopecia

Musculoskeletal

- arthralgia
- non-erosive arthritis

Cardiovascular

- myocarditis

Respiratory

- pleurisy
- fibrosing alveolitis

Renal

- proteinuria
- glomerulonephritis (diffuse proliferative glomerulonephritis is the most common type)

Neuropsychiatric

- anxiety and depression
- psychosis
- seizures

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Systemic lupus erythematosus: investigations



Immunology

- 99% are ANA positive
- 20% are rheumatoid factor positive
- anti-dsDNA: highly specific (> 99%), but less sensitive (70%)
- anti-Smith: most specific (> 99%), sensitivity (30%)
- also: anti-U1 RNP, SS-A (anti-Ro) and SS-B (anti-La)

Monitoring

- ESR: during active disease the CRP is characteristically normal - a raised CRP may indicate underlying infection
- complement levels (C3, C4) are low during active disease (formation of complexes leads to consumption of complement)
- anti-dsDNA titres can be used for disease monitoring (but note not present in all patients)

Systemic lupus erythematosus: investigations



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Systemic lupus erythematosus: pregnancy

Overview

- risk of maternal autoantibodies crossing placenta
- leads to condition termed neonatal lupus erythematosus
- neonatal complications include congenital heart block
- strongly associated with anti-Ro (SSA) antibodies

Next question >

Drug-induced lupus

In drug-induced lupus not all the typical features of systemic lupus erythematosus are seen, with renal and nervous system involvement being unusual. It usually resolves on stopping the drug.

Features

- arthralgia
- myalgia
- skin (e.g. malar rash) and pulmonary involvement (e.g. pleurisy) are common
- ANA positive in 100%, dsDNA negative
- anti-histone antibodies are found in 80-90%
- anti-Ro, anti-Smith positive in around 5%



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A woman with drug-induced lupus

Most common causes

- procainamide
- hydralazine

Less common causes

- isoniazid
- minocycline
- phenytoin

Discoid lupus erythematosus



Discoid lupus erythematosus is a benign disorder generally seen in younger females. It very rarely progresses to systemic lupus erythematosus (in less than 5% of cases). Discoid lupus erythematosus is characterised by follicular keratin plugs and is thought to be autoimmune in aetiology

Features

- erythematous, raised rash, sometimes scaly
- may be photosensitive
- more common on face, neck, ears and scalp
- lesions heal with atrophy, scarring (may cause scarring alopecia), and pigmentation

Management

- topical steroid cream
- oral antimalarials may be used second-line e.g. hydroxychloroquine
- avoid sun exposure



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Discoid lupus erythematosus affecting the scalp

Rheumatoid arthritis: presentation

Typical features

- swollen, painful joints in hands and feet
- stiffness worse in the morning
- gradually gets worse with larger joints becoming involved
- presentation usually insidiously develops over a few months
- positive 'squeeze test' - discomfort on squeezing across the metacarpal or metatarsal joints

Other presentations:

- acute onset with marked systemic disturbance
- relapsing/remitting monoarthritis of different large joints (palindromic rheumatism)

Rheumatoid arthritis: diagnosis

NICE have stated that clinical diagnosis is more important than criteria such as those defined by the American College of Rheumatology.

2010 American College of Rheumatology criteria

Target population. Patients who

- 1) have at least 1 joint with definite clinical synovitis
- 2) with the synovitis not better explained by another disease

Classification criteria for rheumatoid arthritis (add score of categories A-D; a score of 6/10 is needed definite rheumatoid arthritis)

Rheumatoid arthritis: prognostic features

A number of features have been shown to predict a poor prognosis in patients with rheumatoid arthritis, as listed below

Poor prognostic features

- rheumatoid factor positive
- poor functional status at presentation
- HLA DR4
- X-ray: early erosions (e.g. after < 2 years)
- extra articular features e.g. nodules
- insidious onset
- anti-CCP antibodies

In terms of gender there seems to be a split in what the established sources state is associated with a poor prognosis. However both the American College of Rheumatology and the recent NICE guidelines (which looked at a huge number of prognosis studies) seem to conclude that female gender is associated with a poor prognosis.

Key

- RF = rheumatoid factor
- ACPA = anti-cyclic citrullinated peptide antibody

Factor	Scoring	
A. Joint involvement		
	1 large joint	0
	2 - 10 large joints	1
	1 - 3 small joints (with or without involvement of large joints)	2
	4 - 10 small joints (with or without involvement of large joints)	3
	10 joints (at least 1 small joint)	5
B. Serology (at least 1 test result is needed for classification)		
	Negative RF and negative ACPA	0
	Low-positive RF or low-positive ACPA	2
	High-positive RF or high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)		
	Normal CRP and normal ESR	0
	Abnormal CRP or abnormal ESR	1
D. Duration of symptoms		
	< 6 weeks	0
	> 6 weeks	1

Rheumatoid arthritis: complications

A wide variety of extra-articular complications occur in patients with rheumatoid arthritis (RA):

- respiratory: pulmonary fibrosis, pleural effusion, pulmonary nodules, bronchiolitis obliterans, methotrexate pneumonitis, pleurisy
- ocular: keratoconjunctivitis sicca (most common), episcleritis, scleritis, corneal ulceration, keratitis, steroid-induced cataracts, chloroquine retinopathy
- osteoporosis
- ischaemic heart disease: RA carries a similar risk to type 2 diabetes mellitus
- increased risk of infections
- depression

Less common

- Felty's syndrome (RA + splenomegaly + low white cell count)
- amyloidosis



Rheumatoid arthritis: antibodies

Rheumatoid factor

Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patient's own IgG

RF can be detected by either

- Rose-Waaler test: sheep red cell agglutination
- Latex agglutination test (less specific)

RF is positive in 70-80% of patients with rheumatoid arthritis, high titre levels are associated with severe progressive disease (but NOT a marker of disease activity)

Other conditions associated with a positive RF include:

- Sjogren's syndrome (around 100%)
- Felty's syndrome (around 100%)
- infective endocarditis (= 50%)
- SLE (= 20-30%)
- systemic sclerosis (= 30%)
- general population (= 5%)
- rarely: TB, HBV, EBV, leprosy

Anti-cyclic citrullinated peptide antibody

Anti-cyclic citrullinated peptide antibody may be detectable up to 10 years before the development of rheumatoid arthritis. It may therefore play a key role in the future of rheumatoid arthritis, allowing early detection of patients suitable for aggressive anti-TNF therapy. It has a sensitivity similar to rheumatoid factor (around 70%) with a much higher specificity of 90-95%.

NICE recommends that patients with suspected rheumatoid arthritis who are rheumatoid factor negative should be tested for anti-CCP antibodies.

Next question >

Rheumatoid arthritis: management



The management of rheumatoid arthritis (RA) has been revolutionised by the introduction of disease-modifying therapies in the past decade. NICE has issued a number of technology appraisals on the newer agents and released general guidelines in 2009.

Patients with evidence of joint inflammation should start a combination of disease-modifying drugs (DMARD) as soon as possible. Other important treatment options include analgesia, physiotherapy and surgery.

Initial therapy

- in the 2009 NICE guidelines it is recommended that patients with newly diagnosed active RA start a combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids)

DMARDs

- methotrexate is the most widely used DMARD. Monitoring of FBC & LFTs is essential due to the risk of myelosuppression and liver cirrhosis. Other important side-effects include pneumonitis
- sulfasalazine
- leflunomide
- hydroxychloroquine

TNF-inhibitors

- the current indication for a TNF-inhibitor is an inadequate response to at least two DMARDs including methotrexate
- etanercept: recombinant human protein, acts as a decoy receptor for TNF- α , subcutaneous administration, can cause demyelination, risks include reactivation of tuberculosis
- infliximab: monoclonal antibody, binds to TNF- α and prevents it from binding with TNF receptors, intravenous administration, risks include reactivation of tuberculosis
- adalimumab: monoclonal antibody, subcutaneous administration

Rituximab

- anti-CD20 monoclonal antibody, results in B-cell depletion
- two 1g intravenous infusions are given two weeks apart
- infusion reactions are common

Abatacept

- fusion protein that modulates a key signal required for activation of T lymphocytes
- leads to decreased T-cell proliferation and cytokine production
- given as an infusion
- not currently recommended by NICE

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Rheumatoid arthritis: pregnancy

Rheumatoid arthritis (RA) typically develops in women of a reproductive age. Issues surrounding conception are therefore commonly encountered. There are no current published guidelines regarding how patients considering conception should be managed although expert reviews are largely in agreement.

Key points

- patients with early or poorly controlled RA should be advised to defer conception until their disease is more stable
- RA symptoms tend to improve in pregnancy but only resolve in a small minority. Patients tend to have a flare following delivery
- methotrexate is not safe in pregnancy and needs to be stopped at least 3 months before conception
- leflunomide is not safe in pregnancy
- sulfasalazine and hydroxychloroquine are considered safe in pregnancy
- interestingly studies looking at pregnancy outcomes in patients treated with TNF- α blockers do not show any significant increase in adverse outcomes. It should be noted however that many of the patients included in the study stopped taking TNF- α blockers when they found out they were pregnant
- low-dose corticosteroids may be used in pregnancy to control symptoms
- NSAIDs may be used until 32 weeks but after this time should be withdrawn due to the risk of early close of the ductus arteriosus
- patients should be referred to an obstetric anaesthetist due to the risk of atlanto-axial subluxation

Azathioprine

Azathioprine is metabolised to the active compound mercaptopurine, a purine analogue that inhibits purine synthesis. A thiopurine methyltransferase (TPMT) test may be needed to look for individuals prone to azathioprine toxicity.

Adverse effects include

- bone marrow depression
- nausea/vomiting
- pancreatitis

A significant interaction may occur with allopurinol and hence lower doses of azathioprine should be used.

Methotrexate



Methotrexate is an antimetabolite that inhibits dihydrofolate reductase, an enzyme essential for the synthesis of purines and pyrimidines. It is considered an 'important' drug as whilst it can be very effective in controlling disease the side-effects may be potentially life-threatening - careful prescribing and close monitoring is essential.

Indications

- inflammatory arthritis, especially rheumatoid arthritis
- psoriasis
- some chemotherapy acute lymphoblastic leukaemia

Adverse effects

- mucositis
- myelosuppression
- pneumonitis
- pulmonary fibrosis
- liver cirrhosis

Pregnancy

- women should avoid pregnancy for at least 3 months after treatment has stopped
- the BNF also advises that men using methotrexate need to use effective contraception for at least 3 months after treatment

Prescribing methotrexate

- methotrexate is a drug with a high potential for patient harm. It is therefore important that you are familiar with guidelines relating to its use
- methotrexate is taken weekly, rather than daily
- FBC, U&E and LFTs need to be regularly monitored. The Committee on Safety of Medicines recommend 'FBC and renal and LFTs before starting treatment and repeated weekly until therapy stabilised, thereafter patients should be monitored every 2-3 months'
- folic acid 5mg once weekly should be co-prescribed, taken more than 24 hours after methotrexate dose
- the starting dose of methotrexate is 7.5 mg weekly (source: BNF)
- only one strength of methotrexate tablet should be prescribed (usually 2.5 mg)
- avoid prescribing trimethoprim or cotrimoxazole concurrently - increases risk of marrow aplasia



Rheumatoid arthritis: drug side-effects

The table below lists some of the characteristic (if not common) side-effects of drugs used to treat rheumatoid arthritis:

Drug	Side-effects
Methotrexate	Myelosuppression Liver cirrhosis Pneumonitis
Sulfasalazine	Rashes Oligospermia Heinz body anaemia Interstitial lung disease
Leflunomide	Liver impairment Interstitial lung disease Hypertension
Hydroxychloroquine	Retinopathy Corneal deposits
Prednisolone	Cushingoid features Osteoporosis Impaired glucose tolerance Hypertension Cataracts
Gold	Proteinuria
Penicillamine	Proteinuria Exacerbation of myasthenia gravis
Etanercept	Demyelination Reactivation of tuberculosis
Infliximab	Reactivation of tuberculosis
Adalimumab	Reactivation of tuberculosis
Rituximab	Infusion reactions are common
NSAIDs (e.g. naproxen, ibuprofen)	Bronchospasm in asthmatics Dyspepsia/peptic ulceration

Behcet's syndrome



Behcet's syndrome is a complex multisystem disorder associated with presumed autoimmune mediated inflammation of the arteries and veins. The precise aetiology has yet to be elucidated however. The classic triad of symptoms are oral ulcers, genital ulcers and anterior uveitis

Epidemiology

- more common in the eastern Mediterranean (e.g. Turkey)
- more common in men (complicated gender distribution which varies according to country. Overall, Behcet's is considered to be more common and more severe in men)
- tends to affect young adults (e.g. 20 - 40 years old)
- associated with HLA B5* and MICA6 allele
- around 30% of patients have a positive family history

Features

- classically: 1) oral ulcers 2) genital ulcers 3) anterior uveitis
- thrombophlebitis
- arthritis
- neurological involvement (e.g. aseptic meningitis)
- GI: abdo pain, diarrhoea, colitis
- erythema nodosum, DVT

Diagnosis

- no definitive test
- diagnosis based on clinical findings
- positive pathergy test is suggestive (puncture site following needle prick becomes inflamed with small pustule forming)

*more specifically HLA B51, a split antigen of HLA B5

Temporal arteritis



Temporal arteritis is large vessel vasculitis which overlaps with polymyalgia rheumatica (PMR). Histology shows changes which characteristically 'skips' certain sections of affected artery whilst damaging others.

Features

- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- headache (found in 85%)
- jaw claudication (65%)
- visual disturbances secondary to anterior ischemic optic neuropathy
- tender, palpable temporal artery
- features of PMR: aching, morning stiffness in proximal limb muscles (not weakness)
- also lethargy, depression, low-grade fever, anorexia, night sweats

Investigations

- raised inflammatory markers: ESR > 50 mm/hr (note ESR < 30 in 10% of patients). CRP may also be elevated
- temporal artery biopsy: skip lesions may be present
- note creatine kinase and EMG normal

Treatment

- high-dose prednisolone - there should be a dramatic response, if not the diagnosis should be reconsidered
- urgent ophthalmology review. Patients with visual symptoms should be seen the same-day by an ophthalmologist. Visual damage is often irreversible

Sjogren's syndrome

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

Features

- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

Investigation

- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

Management

- artificial saliva and tears
 - pilocarpine may stimulate saliva production
-

Reactive arthritis: features

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. It encompasses Reiter's syndrome, a term which described a classic triad of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection (post-STI, now sometimes referred to as sexually acquired reactive arthritis, SARA).

Reactive arthritis is defined as an arthritis that develops following an infection where the organism cannot be recovered from the joint.

Features

- typically develops within 4 weeks of initial infection - symptoms generally last around 4-6 months
- arthritis is typically an asymmetrical oligoarthritis of lower limbs
- dactylitis
- symptoms of urethritis
- eye: conjunctivitis (seen in 50%), anterior uveitis
- skin: circinate balanitis (painless vesicles on the coronal margin of the prepuce), keratoderma blennorrhagica (waxy yellow/brown papules on palms and soles)

Around 25% of patients have recurrent episodes whilst 10% of patients develop chronic disease

'Can't see, pee or climb a tree'



Keratoderma blennorrhagica

Bone disorders: lab values

Disorder	Calcium	Phosphate	ALP	PTH
Osteoporosis	Normal	Normal	Normal	Normal
Osteomalacia	Decreased	Decreased	Increased	Increased
Primary hyperparathyroidism (→ osteitis fibrosa cystica)	Increased	Decreased	Increased	Increased
Chronic kidney disease (→ secondary hyperparathyroidism)	Decreased	Increased	Increased	Increased
Paget's disease	Normal	Normal	Increased	Normal
Osteopetrosis	Normal	Normal	Normal	Normal

Gout: predisposing factors

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Decreased excretion of uric acid

- drugs*: diuretics
- chronic kidney disease
- lead toxicity

Increased production of uric acid

- myeloproliferative/lymphoproliferative disorder
- cytotoxic drugs
- severe psoriasis

Lesch-Nyhan syndrome

- hypoxanthine-guanine phosphoribosyl transferase (HGPRTase) deficiency
- x-linked recessive therefore only seen in boys
- features: gout, renal failure, neurological deficits, learning difficulties, self-mutilation

*aspirin in a dose of 75-150mg is not thought to have a significant effect on plasma urate levels - the British Society for Rheumatology recommend it should be continued if required for cardiovascular prophylaxis

[Next question >](#)

Gout: drug causes

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Drug causes

- thiazides, furosemide
 - alcohol
 - cytotoxic agents
 - pyrazinamide
-

Gout: features

Gout is a form of inflammatory arthritis. Patients typically have episodes lasting several days when their gout flares and are often symptom free between episodes. The acute episodes typically develop maximal intensity within 12 hours. The main features it presents with are:

- pain: this is often very significant
- swelling
- erythema

Around 70% of first presentations affect the 1st metatarsophalangeal (MTP) joint. Attacks of gout affecting this area were historically called podagra. Other commonly affected joints include:

- ankle
- wrist
- knee

If untreated repeated acute episodes of gout can damage the joints resulting in a more chronic joint problem.

Radiological features of gout include:

- joint effusion is an early sign
- well-defined 'punched-out' erosions with sclerotic margins in a juxta-articular distribution, often with overhanging edges
- relative preservation of joint space until late disease
- eccentric erosions
- no periarticular osteopaenia (in contrast to rheumatoid arthritis)
- soft tissue tophi may be seen



Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450 $\mu\text{mol/l}$)

Acute management

- NSAIDs
- intra-articular steroid injection
- colchicine* has a slower onset of action. The main side-effect is diarrhoea
- oral steroids may be considered if NSAIDs and colchicine are contraindicated. A dose of prednisolone 15mg/day is usually used
- if the patient is already taking allopurinol it should be continued

Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300 $\mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol**

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

Other points

- losartan has a specific uricosuric action and may be particularly suitable for the many patients who have coexistent hypertension
- calcium channel blockers also decrease uric acid levels, possibly by a renal vasodilatory effect
- increased vitamin C intake (either supplements or through normal diet) may also decrease serum uric acid levels

*inhibits microtubule polymerization by binding to tubulin, interfering with mitosis. Also inhibits neutrophil motility and activity

**patients with Lesch-Nyhan syndrome often take allopurinol for life

Pseudogout

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

Risk factors

- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

Features

- knee, wrist and shoulders most commonly affected
- joint aspiration: weakly-positively birefringent rhomboid shaped crystals
- x-ray: chondrocalcinosis

Management

- aspiration of joint fluid, to exclude septic arthritis
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout



Osteomalacia

Basics

- normal bony tissue but decreased mineral content
- rickets if when growing
- osteomalacia if after epiphysis fusion

Types

- vitamin D deficiency e.g. malabsorption, lack of sunlight, diet
- renal failure
- drug induced e.g. anticonvulsants
- vitamin D resistant; inherited
- liver disease, e.g. cirrhosis

Features

- rickets: knock-knee, bow leg, features of hypocalcaemia
- osteomalacia: bone pain, fractures, muscle tenderness, proximal myopathy

Investigation

- low calcium, phosphate, 25(OH) vitamin D
- raised alkaline phosphatase
- x-ray: children - cupped, ragged metaphyseal surfaces; adults - translucent bands (Looser's zones or pseudofractures)

Treatment

- calcium with vitamin D tablets

Osteomyelitis

Osteomyelitis describes an infection of the bone.

Staph. aureus is the most common cause except in patients with sickle-cell anaemia where *Salmonella* species predominate.

Predisposing conditions

- diabetes mellitus
- sickle cell anaemia
- intravenous drug user
- immunosuppression due to either medication or HIV
- alcohol excess

Investigations

- MRI is the imaging modality of choice, with a sensitivity of 90-100%

Management

- flucloxacillin for 6 weeks
- clindamycin if penicillin-allergic

McArdle's disease

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Overview

- autosomal recessive type V glycogen storage disease
- caused by myophosphorylase deficiency
- this causes decreased muscle glycogenolysis

Features

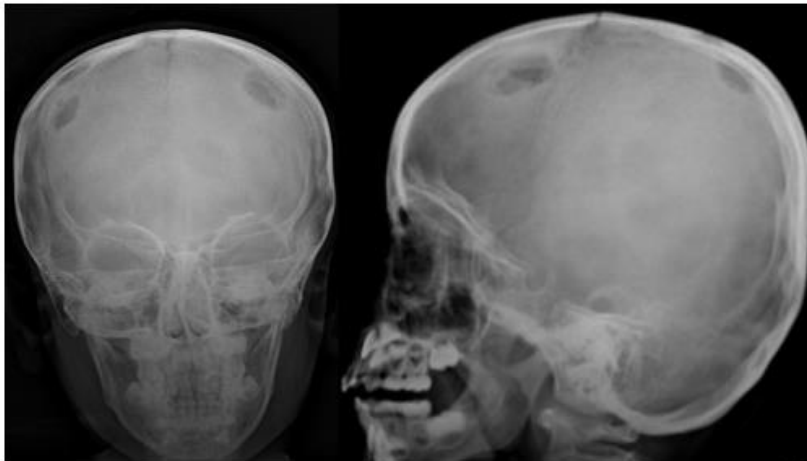
- muscle pain and stiffness following exercise
- muscle cramps
- myoglobinuria
- low lactate levels during exercise

Langerhans cell histiocytosis

Langerhans cell histiocytosis is a rare condition associated with the abnormal proliferation of histiocytes. It typically presents in childhood with bony lesions.

Features

- bone pain, typically in the skull or proximal femur
- cutaneous nodules
- recurrent otitis media/mastoiditis
- tennis racket-shaped Birbeck granules on electromicroscopy



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Young girl with multiple well defined 'punched out' osteolytic lesions with scalloped edges (geographic skull) are seen in the bilateral parietal regions. The lesions have a characteristic bevelled edge.

Osteogenesis imperfecta

Osteogenesis imperfecta (more commonly known as brittle bone disease) is a group of disorders of collagen metabolism resulting in bone fragility and fractures. The most common, and milder, form of osteogenesis imperfecta is type 1

Overview

- autosomal dominant
- abnormality in type 1 collagen due to decreased synthesis of pro-alpha 1 or pro-alpha 2 collagen polypeptides

Features

- presents in childhood
- fractures following minor trauma
- blue sclera
- deafness secondary to otosclerosis
- dental imperfections are common

Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15 and affects around 1 in 3,000 people.

Features

- tall stature with arm span to height ratio > 1.05
- high-arched palate
- arachnodactyly
- pectus excavatum
- pes planus
- scoliosis of > 20 degrees
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic aneurysm, aortic dissection, aortic regurgitation, mitral valve prolapse (75%),
- lungs: repeated pneumothoraces
- eyes: upwards lens dislocation (superotemporal ectopia lentis), blue sclera, myopia
- dural ectasia (ballooning of the dural sac at the lumbosacral level)

The life expectancy of patients used to be around 40-50 years. With the advent of regular echocardiography monitoring and beta-blocker/ACE-inhibitor therapy this has improved significantly over recent years. Aortic dissection and other cardiovascular problems remain the leading cause of death however.



Ehler-Danlos syndrome

Ehler-Danlos syndrome is an autosomal dominant connective tissue disorder that mostly affects type III collagen. This results in the tissue being more elastic than normal leading to joint hypermobility and increased elasticity of the skin.

Features and complications

- elastic, fragile skin
- joint hypermobility: recurrent joint dislocation
- easy bruising
- aortic regurgitation, mitral valve prolapse and aortic dissection
- subarachnoid haemorrhage
- angioid retinal streaks

Bone tumours

Benign tumours

Tumour	Notes
Osteoma	• benign 'overgrowth' of bone, most typically occurring on the skull • associated with Gardner's syndrome (a variant of familial adenomatous polyposis, FAP)
Osteochondroma (exostosis)	• most common benign bone tumour • more in males, usually diagnosed in patients aged < 20 years • cartilage-capped bony projection on the external surface of a bone
Giant cell tumour	• tumour of multinucleated giant cells within a fibrous stroma • peak incidence: 20-40 years • occurs most frequently in the epiphyses of long bones • X-ray shows a 'double bubble' or 'soap bubble' appearance

Malignant tumours

Tumour	Notes
Osteosarcoma	• most common primary malignant bone tumour • seen mainly in children and adolescents • occurs most frequently in the metaphyseal region of long bones prior to epiphyseal closure, with 40% occurring in the femur, 20% in the tibia, and 10% in the humerus • x-ray shows Codman triangle (from periosteal elevation) and 'sunburst' pattern • mutation of the Rb gene significantly increases risk of osteosarcoma (hence association with retinoblastoma) • other predisposing factors include Paget's disease of the bone and radiotherapy
Ewing's sarcoma	• small round blue cell tumour • seen mainly in children and adolescents • occurs most frequently in the pelvis and long bones. Tends to cause severe pain • associated with t(11;22) translocation which results in an EWS-FLI1 gene product • x-ray shows 'onion skin' appearance
Chondrosarcoma	• malignant tumour of cartilage • most commonly affects the axial skeleton • more common in middle-age



Chronic fatigue syndrome

Diagnosed after at least 4 months of disabling fatigue affecting mental and physical function more than 50% of the time in the absence of other disease which may explain symptoms

Epidemiology

- more common in females
- past psychiatric history has not been shown to be a risk factor

Fatigue is the central feature, other recognised features include

- sleep problems, such as insomnia, hypersomnia, unrefreshing sleep, a disturbed sleep-wake cycle
- muscle and/or joint pains
- headaches
- painful lymph nodes without enlargement
- sore throat
- cognitive dysfunction, such as difficulty thinking, inability to concentrate, impairment of short-term memory, and difficulties with word-finding
- physical or mental exertion makes symptoms worse
- general malaise or 'flu-like' symptoms
- dizziness
- nausea
- palpitations

Investigation

- NICE guidelines suggest carrying out a large number of screening blood tests to exclude other pathology e.g. FBC, U&E, LFT, glucose, TFT, ESR, CRP, calcium, CK, ferritin*, coeliac screening and also urinalysis

Management

- cognitive behaviour therapy - very effective, number needed to treat = 2
- graded exercise therapy - a formal supervised program, not advice to go to the gym
- 'pacing' - organising activities to avoid tiring
- low-dose amitriptyline may be useful for poor sleep
- referral to a pain management clinic if pain is a predominant feature

Better prognosis in children

*children and young people only



Hip problems in children

The table below provides a brief summary of the potential causes of hip problems in children

Condition	Notes
Development dysplasia of the hip	Often picked up on newborn examination Barlow's test, Ortolani's test are positive Unequal skin folds/leg length
Transient synovitis (irritable hip)	Typical age group = 2-10 years Acute hip pain associated with viral infection Commonest cause of hip pain in children
Perthes disease	Perthes disease is a degenerative condition affecting the hip joints of children, typically between the ages of 4-8 years. It is due to avascular necrosis of the femoral head Perthes disease is 5 times more common in boys. Around 10% of cases are bilateral Features • hip pain: develops progressively over a few weeks • limp • stiffness and reduced range of hip movement • x-ray: early changes include widening of joint space, later changes include decreased femoral head size/flattening
Slipped upper femoral epiphysis	Typical age group = 10-15 years More common in obese children and boys Displacement of the femoral head epiphysis postero-inferiorly Bilateral slip in 20% of cases May present acutely following trauma or more commonly with chronic, persistent symptoms Features • knee or distal thigh pain is common • loss of internal rotation of the leg in flexion

Juvenile idiopathic arthritis (JIA)	Preferred to the older term juvenile chronic arthritis, describes arthritis occurring in someone who is less than 16 years old that lasts for more than three months. Pauciarticular JIA refers to cases where 4 or less joints are affected. It accounts for around 60% of cases of JIA Features of pauciarticular JIA • joint pain and swelling: usually medium sized joints e.g. knees, ankles, elbows • limp • ANA may be positive in JIA - associated with anterior uveitis
Septic arthritis	Acute hip pain associated with systemic upset e.g. pyrexia. Inability/severe limitation of affected joint

Image gallery



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Perthes disease - both femoral epiphyses show extensive destruction, the acetabula are deformed



Avascular necrosis

Avascular necrosis (AVN) may be defined as death of bone tissue secondary to loss of the blood supply. This leads to bone destruction and loss of joint function. It most commonly affects the epiphysis of long bones such as the femur.

Causes

- long-term steroid use
- chemotherapy
- alcohol excess
- trauma

Features

- initially asymptomatic
- pain in the affected joint

Investigation

- plain x-ray findings may be normal initially
- MRI is the investigation of choice. It is more sensitive than radionuclide bone scanning

Management

- joint replacement may be necessary

Myopathies

Features

- symmetrical muscle weakness (proximal > distal)
- common problems are rising from chair or getting out of bath
- sensation normal, reflexes normal, no fasciculation

Causes

- inflammatory: polymyositis
- inherited: Duchenne/Becker muscular dystrophy, myotonic dystrophy
- endocrine: Cushing's, thyrotoxicosis
- alcohol

Systemic sclerosis



Systemic sclerosis is a condition of unknown aetiology characterised by hardened, sclerotic skin and other connective tissues. It is four times more common in females

There are three patterns of disease:

Limited cutaneous systemic sclerosis

- Raynaud's may be first sign
- scleroderma affects face and distal limbs predominately
- associated with anti-centromere antibodies
- a subtype of limited systemic sclerosis is CREST syndrome: Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly, Telangiectasia

Diffuse cutaneous systemic sclerosis

- scleroderma affects trunk and proximal limbs predominately
- associated with scl-70 antibodies
- hypertension, lung fibrosis and renal involvement seen
- poor prognosis

Scleroderma (without internal organ involvement)

- tightening and fibrosis of skin
- may be manifest as plaques (morphoea) or linear



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Polyarteritis nodosa

Polyarteritis nodosa (PAN) is a vasculitis affecting medium-sized arteries with necrotizing inflammation leading to aneurysm formation. PAN is more common in middle-aged men and is associated with hepatitis B infection.

Features

- fever, malaise, arthralgia
- weight loss
- hypertension
- mononeuritis multiplex, sensorimotor polyneuropathy
- testicular pain
- livedo reticularis
- haematuria, renal failure
- perinuclear-antineutrophil cytoplasmic antibodies (ANCA) are found in around 20% of patients with 'classic' PAN
- hepatitis B serology positive in 30% of patients



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Livedo reticularis

Dermatomyositis

Overview

- an inflammatory disorder causing symmetrical, proximal muscle weakness and characteristic skin lesions
- may be idiopathic or associated with connective tissue disorders or underlying malignancy (typically ovarian, breast and lung cancer, found in 20-25% - more if patient older)
- polymyositis is a variant of the disease where skin manifestations are not prominent

Skin features

- photosensitive
- macular rash over back and shoulder
- heliotrope rash in the periorbital region
- Gottron's papules - roughened red papules over extensor surfaces of fingers
- nail fold capillary dilatation

Other features

- proximal muscle weakness +/- tenderness
- Raynaud's
- respiratory muscle weakness
- interstitial lung disease: e.g. Fibrosing alveolitis or organising pneumonia
- dysphagia, dysphonia

Investigations

- the majority of patients are ANA positive, with around 25% anti-Mi-2 positive

[Next question >](#)

Dermatomyositis: investigations and management

Investigations

- elevated creatine kinase
- EMG
- muscle biopsy
- ANA positive in 60%
- anti-Mi-2 antibodies are highly specific for dermatomyositis, but are only seen in around 25% of patients
- anti-Jo-1 antibodies are not commonly seen in dermatomyositis - they are more common in polymyositis where they are seen in a pattern of disease associated with lung involvement, Raynaud's and fever

Management

- prednisolone

[Next question >](#)

Dermatomyositis: investigations and management

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Management

- prednisolone

Polymyositis



Overview

- inflammatory disorder causing symmetrical, proximal muscle weakness
- thought to be a T-cell mediated cytotoxic process directed against muscle fibres
- may be idiopathic or associated with connective tissue disorders
- associated with malignancy
- dermatomyositis is a variant of the disease where skin manifestations are prominent, for example a purple (heliotrope) rash on the cheeks and eyelids
- typically affects middle-aged, female: male 3:1

Features

- proximal muscle weakness +/- tenderness
- Raynaud's
- respiratory muscle weakness
- interstitial lung disease: e.g. fibrosing alveolitis or organising pneumonia
- dysphagia, dysphonia

Investigations

- elevated creatine kinase
- EMG
- muscle biopsy
- anti-Jo-1 antibodies are seen in pattern of disease associated with lung involvement, Raynaud's and fever

Raynaud's



Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease

- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthritis or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes

- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management

- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months



Polymyalgia rheumatica

Pathophysiology

- overlaps with temporal arteritis
- histology shows vasculitis with giant cells, characteristically 'skips' certain sections of affected artery whilst damaging others
- muscle bed arteries affected most in polymyalgia rheumatica

Features

- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- aching, morning stiffness in proximal limb muscles (not weakness)
- also mild polyarthralgia, lethargy, depression, low-grade fever, anorexia, night sweats

Investigations

- ESR > 40 mm/hr
- note CK and EMG normal
- reduced CD8+ T cells

Treatment

- prednisolone e.g. 15mg/od - dramatic response

Ankylosing spondylitis: investigation and management

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 3:1) aged 20-30 years old.

Investigation

Inflammatory markers (ESR, CRP) are typically raised although normal levels do not exclude ankylosing spondylitis.

HLA-B27 is of little use in making the diagnosis as it is positive in:

- 90% of patients with ankylosing spondylitis
- 10% of normal patients

Plain x-ray of the sacroiliac joints is the most useful investigation in establishing the diagnosis. Radiographs may be normal early in disease, later changes include:

- sacroilitis: subchondral erosions, sclerosis
- squaring of lumbar vertebrae
- 'bamboo spine' (late & uncommon)
- syndesmophytes: due to ossification of outer fibers of annulus fibrosus
- chest x-ray: apical fibrosis





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Syndesmophytes and squaring of vertebral bodies. Squaring of anterior vertebral margins is due to osteitis of anterior corners. Syndesmophytes are due to ossification of outer fibers of annulus fibrosus

Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints.

Management

The following is partly based on the 2010 EULAR guidelines (please see the link for more details):

- encourage regular exercise such as swimming
- physiotherapy
- NSAIDs are the first-line treatment
- the disease-modifying drugs which are used to treat rheumatoid arthritis (such as sulphasalazine) are only really useful if there is peripheral joint involvement
- the 2010 EULAR guidelines suggest: '*Anti-TNF therapy should be given to patients with persistently high disease activity despite conventional treatments*'
- research is ongoing to see whether anti-TNF therapies such as etanercept and adalimumab should be used earlier in the course of the disease

Osteoporosis: causes

Advancing age and female sex are significant risk factors for osteoporosis. Prevalence of osteoporosis increases from 2% at 50 years to more than 25% at 80 years in women.

There are many other risk factors and secondary causes of osteoporosis. We'll start by looking at the most 'important' ones - these are risk factors that are used by major risk assessment tools such as FRAX:

- history of glucocorticoid use
- rheumatoid arthritis
- alcohol excess
- history of parental hip fracture
- low body mass index
- current smoking

Other risk factors

- sedentary lifestyle
- premature menopause
- Caucasians and Asians
- endocrine disorders: hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- gastrointestinal disorders: inflammatory bowel disease, malabsorption (e.g. Coeliac's), gastrectomy, liver disease
- chronic kidney disease
- osteogenesis imperfecta, homocystinuria

Medications that may worsen osteoporosis (other than glucocorticoids):

- SSRIs
- antiepileptics
- proton pump inhibitors
- glitazones
- long term heparin therapy
- aromatase inhibitors e.g. anastrozole

Investigations for secondary causes

Next question >

Osteoporosis: DEXA scan

Basics

- T score: based on bone mass of young reference population
- T score of -1.0 means bone mass of one standard deviation below that of young reference population
- Z score is adjusted for age, gender and ethnic factors

T score

- > -1.0 = normal
- -1.0 to -2.5 = osteopaenia
- < -2.5 = osteoporosis

Next question >

Bisphosphonates



Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis.

Clinical uses

- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metastases

Adverse effects

- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw
- increased risk of atypical stress fractures of the proximal femoral shaft in patients taking alendronate
- acute phase response: fever, myalgia and arthralgia may occur following administration
- hypocalcaemia: due to reduced calcium efflux from bone. Usually clinically unimportant

The BNF suggests the following counselling for patients taking oral bisphosphonates

- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'

The duration of bisphosphonate treatment varies according to the level of risk. Some authorities recommend stopping bisphosphonates at 5 years if the following apply:

- patient is < 75-years-old
- femoral neck T-score of > -2.5
- low risk according to FRAX/NOGG

ANCA



Question

A 25-year-old male patient is noted to have

Rheumatoid arthritis

Ehler-Danlos syndrome

Homocystinuria

Reactive arthritis

Marfan syndrome

Polymyositis

42 facts

Score for this question

6 in a row

Key facts

There are two main types of anti-neutrophil cytoplasmic antibodies (ANCA) - cytoplasmic (cANCA) and perinuclear (pANCA)

For the exam, remember:

- cANCA - granulomatosis with polyangiitis (Wegener's granulomatosis)
- pANCA - Churg-Strauss syndrome + others (see below)

cANCA

- most common target serine proteinase 3 (PR3)
- some correlation between cANCA levels and disease activity
- granulomatosis with polyangiitis, positive in > 90%
- microscopic polyangiitis, positive in 40%

pANCA

- most common target is myeloperoxidase (MPO)
- cannot use level of pANCA to monitor disease activity
- associated with immune crescentic glomerulonephritis (positive in c. 80% of patients)
- microscopic polyangiitis, positive in 50-75%
- Churg-Strauss syndrome, positive in 60%
- primary sclerosing cholangitis, positive in 60-80%
- granulomatosis with polyangiitis, positive in 25%

Other causes of positive ANCA (usually pANCA)

- inflammatory bowel disease (UC > Crohn's)
- connective tissue disorders: RA, SLE, Sjogren's
- autoimmune hepatitis

Investigations for secondary causes

If a patient is diagnosed with osteoporosis or has a fragility fracture further investigations may be warranted. NOGG recommend testing for the following reasons:

- exclude diseases that mimic osteoporosis (e.g. osteomalacia, myeloma);
- identify the cause of osteoporosis and contributory factors;
- assess the risk of subsequent fractures;
- select the most appropriate form of treatment

The following investigations are recommended by NOGG:

- History and physical examination
- Blood cell count, sedimentation rate or C-reactive protein, serum calcium,

albumin, creatinine, phosphate, alkaline phosphatase and liver transaminases

- Thyroid function tests
- Bone densitometry (DXA)

Other procedures, if indicated

- Lateral radiographs of lumbar and thoracic spine/DXA-based vertebral imaging
- Protein immunoelectrophoresis and urinary Bence-Jones proteins
- 25OHD
- PTH
- Serum testosterone, SHBG, FSH, LH (in men),
- Serum prolactin
- 24 hour urinary cortisol/dexamethasone suppression test
- Endomysial and/or tissue transglutaminase antibodies (coeliac disease)
- Isotope bone scan
- Markers of bone turnover, when available
- Urinary calcium excretion

So from the first list we should order the following bloods as a minimum for all patients:

- full blood count
- urea and electrolytes
- liver function tests
- bone profile
- CRP
- thyroid function tests

Hydroxychloroquine

Hydroxychloroquine is used in the management of rheumatoid arthritis and systemic/discoid lupus erythematosus. It is pharmacologically very similar to chloroquine which is used to treat certain types of malaria.

Adverse effects

- bull's eye retinopathy - may result in severe and permanent visual loss

Monitoring

- the BNF advises: *'Ask patient about visual symptoms and monitor visual acuity annually using the standard reading chart'*

Next question >

B I

Leflunomide

Leflunomide is a disease modifying anti-rheumatic drug (DMARD) mainly used in the management of rheumatoid arthritis. It has a very long half-life which should be remembered considering its teratogenic potential.

Contraindications

- pregnancy - the BNF advises: *'Effective contraception essential during treatment and for at least 2 years after treatment in women and at least 3 months after treatment in men (plasma concentration monitoring required)'*
- caution should also be exercised with pre-existing lung and liver disease

Adverse effects

- gastrointestinal, especially diarrhoea
- hypertension
- weight loss/anorexia
- peripheral neuropathy
- myelosuppression
- pneumonitis

Monitoring

- FBC/LFT and blood pressure
- 

Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

Features

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines

- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

[Next question >](#)

Adhesive capsulitis

Adhesive capsulitis (frozen shoulder) is a common cause of shoulder pain. It is most common in middle-aged females. The aetiology of frozen shoulder is not fully understood.

Associations

- diabetes mellitus: up to 20% of diabetics may have an episode of frozen shoulder

Features typically develop over days

- external rotation is affected more than internal rotation or abduction
- both active and passive movement are affected
- patients typically have a painful freezing phase, an adhesive phase and a recovery phase
- bilateral in up to 20% of patients
- the episode typically lasts between 6 months and 2 years

Management

- no single intervention has been shown to improve outcome in the long-term
- treatment options include NSAIDs, physiotherapy, oral corticosteroids and intra-articular corticosteroids

Next question >

Vitamin D supplementation

Vitamin D supplementation has been a hot topic for a number of years now. The muddled waters are now slightly clearer following the release of the following:

- 2012: letter by the Chief Medical Officer regarding vitamin D supplementation
- 2013: National Osteoporosis Society (NOS) release UK Vitamin D guideline

The following groups should be advised to take vitamin D supplementation:

- all pregnant and breastfeeding women should take a daily supplement containing 10µg of vitamin D
- all children aged 6 months - 5 years. Babies fed with formula milk do not need to take a supplement if they are taking more than 500ml of milk a day, as formula milk is fortified with vitamin D
- adults > 65 years
- 'people who are not exposed to much sun should also take a daily supplement'

Testing for vitamin D deficiency

The key message is that not many people warrant a vitamin D test. The NOS guidelines specify that testing may be appropriate in the following situations:

- patients with bone diseases that may be improved with vitamin D treatment e.g. known osteomalacia or Paget's disease
- patients with bone diseases, prior to specific treatment where correcting vitamin deficiency is appropriate e.g. prior to intravenous zoledronate or denosumab
- patients with musculoskeletal symptoms that could be attributed to vitamin D deficiency e.g. bone pain ?osteomalacia

Patients with osteoporosis should always be given calcium/vitamin D supplements so testing is not considered necessary. People who are at higher risk of vitamin D deficiency (see above) should be treated anyway so again testing is not necessary.

Tumour necrosis factor

Tumour necrosis factor (TNF) is a pro-inflammatory cytokine with multiple roles in the immune system

TNF is secreted mainly by macrophages and has a number of effects on the immune system, acting mainly in a paracrine fashion:

- activates macrophages and neutrophils
- acts as costimulator for T cell activation
- key mediator of body's response to Gram negative septicemia
- similar properties to IL-1
- anti-tumour effect (e.g. phospholipase activation)

TNF- α binds to both the p55 and p75 receptor. These receptors can induce apoptosis. It also causes activation of NF κ B

Endothelial effects include increased expression of selectins and increased production of platelet activating factor, IL-1 and prostaglandins

TNF promotes the proliferation of fibroblasts and their production of protease and collagenase. It is thought fragments of receptors act as binding points in serum

Systemic effects include pyrexia, increased acute phase proteins and disordered metabolism leading to cachexia

TNF is important in the pathogenesis of rheumatoid arthritis - TNF blockers (e.g. infliximab, etanercept) are now licensed for treatment of severe rheumatoid

TNF blockers

- infliximab: monoclonal antibody, IV administration
- etanercept: fusion protein that mimics the inhibitory effects of naturally occurring soluble TNF receptors, subcutaneous administration
- adalimumab: monoclonal antibody, subcutaneous administration
- adverse effects of TNF blockers include reactivation of latent tuberculosis and demyelination

Infliximab is also used in active Crohn's disease unresponsive to steroids

Elbow pain

The table below details some of the characteristic features of conditions causing elbow pain:

Lateral epicondylitis (tennis elbow)	Features • pain and tenderness localised to the lateral epicondyle • pain worse on resisted wrist extension with the elbow extended or supination of the forearm with the elbow extended • episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks
Medial epicondylitis (golfer's elbow)	Features • pain and tenderness localised to the medial epicondyle • pain is aggravated by wrist flexion and pronation • symptoms may be accompanied by numbness / tingling in the 4th and 5th finger due to ulnar nerve involvement

Radial tunnel syndrome	Most commonly due to compression of the posterior interosseous branch of the radial nerve. It is thought to be a result of overuse. Features • symptoms are similar to lateral epicondylitis making it difficult to diagnose • however, the pain tends to be around 4-5 cm distal to the lateral epicondyle • symptoms may be worsened by extending the elbow and pronating the forearm
Cubital tunnel syndrome	Due to the compression of the ulnar nerve. Features • initially intermittent tingling in the 4th and 5th finger • may be worse when the elbow is resting on a firm surface or flexed for extended periods • later numbness in the 4th and 5th finger with associated weakness
Olecranon bursitis	Swelling over the posterior aspect of the elbow. There may be associated pain, warmth and erythema. It typically affects middle-aged male patients.

[Next question >](#)

Lateral epicondylitis

Lateral epicondylitis typically follows unaccustomed activity such as house painting or playing tennis ('tennis elbow'). It is most common in people aged 45-55 years and typically affects the dominant arm.

Features

- pain and tenderness localised to the lateral epicondyle
- pain worse on wrist extension against resistance with the elbow extended or supination of the forearm with the elbow extended
- episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks

Management options

- advice on avoiding muscle overload
- simple analgesia
- steroid injection
- physiotherapy

Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2014

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with NSAIDs and COX-2 inhibitors. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended
- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness

[Next question >](#)

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Carpal tunnel syndrome

Carpal tunnel syndrome is caused by compression of median nerve in the carpal tunnel.

History

- pain/pins and needles in thumb, index, middle finger
- unusually the symptoms may 'ascend' proximally
- patient shakes his hand to obtain relief, classically at night

Examination

- weakness of thumb abduction (abductor pollicis brevis)
- wasting of thenar eminence (NOT hypothenar)
- Tinel's sign: tapping causes paraesthesia
- Phalen's sign: flexion of wrist causes symptoms

Causes

- idiopathic
- pregnancy
- oedema e.g. heart failure
- lunate fracture
- rheumatoid arthritis

Electrophysiology

- motor + sensory: prolongation of the action potential

Treatment

- corticosteroid injection
- wrist splints at night
- surgical decompression (flexor retinaculum division)

Next question >

Familial Mediterranean Fever

Familial Mediterranean Fever (FMF, also known as recurrent polyserositis) is an autosomal recessive disorder which typically presents by the second decade. It is more common in people of Turkish, Armenian and Arabic descent

Features - attacks typically last 1-3 days

- pyrexia
- abdominal pain (due to peritonitis)
- pleurisy
- pericarditis
- arthritis
- erysipeloid rash on lower limbs

Management

- colchicine may help

Next question >

Psoriatic arthropathy

Psoriatic arthropathy correlates poorly with cutaneous psoriasis and often precedes the development of skin lesions. Around 10-20% percent of patients with skin lesions develop an arthropathy with males and females being equally affected

Types*

- rheumatoid-like polyarthritis: (30-40%, most common type)
- asymmetrical oligoarthritis: typically affects hands and feet (20-30%)
- sacroilitis
- DIP joint disease (10%)
- arthritis mutilans (severe deformity fingers/hand, 'telescoping fingers')

Management

- treat as rheumatoid arthritis
- but better prognosis



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Notice the nail changes on this image as well

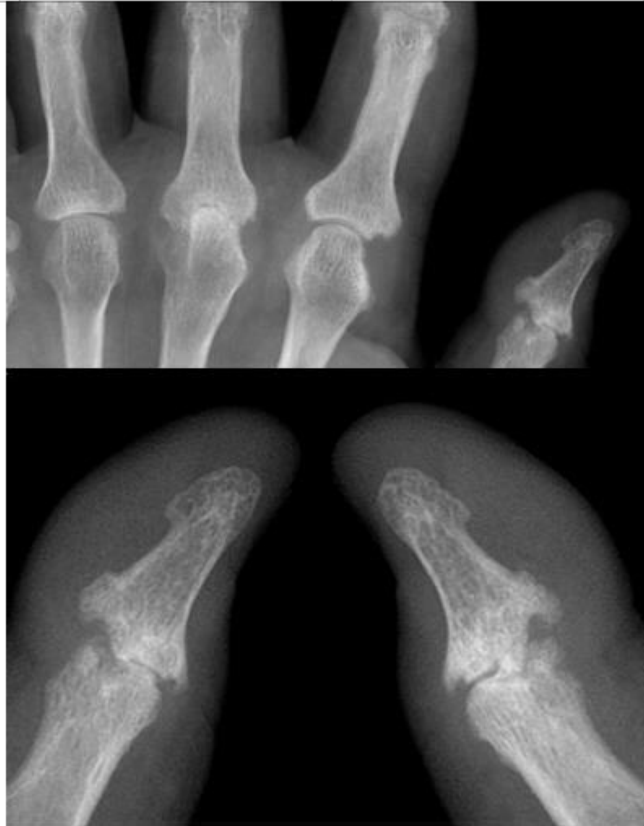


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X-ray showing some of changes in seen in psoriatic arthropathy. Note that the DIPs are predominately affected, rather than the MCPs and PIPs as would be seen with rheumatoid. Extensive juxta-articular periostitis is seen in the DIPs but the changes have not yet progressed to the classic 'pencil-in-cup' changes that are often seen.





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This x-ray shows changes affecting both the PIPs and DIPs. The close-up images show extensive changes including large eccentric erosions, tuft resorption and progression towards a 'pencil-in-cup' changes.

*Until recently it was thought asymmetrical oligoarthritis was the most common type, based on data from the original 1973 Moll and Wright paper. Please see the link for a comparison of more recent studies

[Link to Moll and Wright paper](#)

Next question >

Common peroneal nerve lesion

The sciatic nerve divides into the tibial and common peroneal nerves. Injury often occurs at the neck of the fibula

The most characteristic feature of a common peroneal nerve lesion is foot drop

Other features include:

- weakness of foot dorsiflexion
- weakness of foot eversion
- weakness of extensor hallucis longus
- sensory loss over the dorsum of the foot and the lower lateral part of the leg
- wasting of the anterior tibial and peroneal muscles

Next question >

Rotator cuff muscles

SITS - small t for teres minor

Supraspinatus

Infraspinatus

teres minor

Subscapularis

Muscle	Notes
Supraspinatus	aBDucts arm before deltoid Most commonly injured
Infraspinatus	Rotates arm laterally
teres minor	aDDucts & rotates arm laterally
Subscapularis	aDDuct & rotates arm medially

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Lumbar spinal stenosis

Lumbar spinal stenosis is a condition in which the central canal is narrowed by tumour, disk prolapse or other similar degenerative changes.

Patients may present with a combination of back pain, neuropathic pain and symptoms mimicking claudication. One of the main features that may help to differentiate it from true claudication in the history is the positional element to the pain. Sitting is better than standing and patients may find it easier to walk uphill rather than downhill. The neurogenic claudication type history makes lumbar spinal stenosis a likely underlying diagnosis, the absence of such symptoms makes it far less likely.

Pathology

Degenerative disease is the commonest underlying cause. Degeneration is believed to begin in the intervertebral disk where biochemical changes such as cell death and loss of proteoglycan and water content lead to progressive disk bulging and collapse. This process leads to an increased stress transfer to the posterior facet joints, which accelerates cartilaginous degeneration, hypertrophy, and osteophyte formation; this is associated with thickening and distortion of the ligamentum flavum. The combination of the ventral disk bulging, osteophyte formation at the dorsal facet, and ligamentum flavum hypertrophy combine to circumferentially narrow the spinal canal and the space available for the neural elements. The compression of the nerve roots of the cauda equina leads to the characteristic clinical signs and symptoms of lumbar spinal stenosis.

Diagnosis

MRI scanning is the best modality for demonstrating the canal narrowing. Historically a bicycle test was used as true vascular claudicants could not complete the test.

Treatment

Laminectomy



Lower back pain: prolapsed disc

A prolapsed lumbar disc usually produces clear dermatomal leg pain associated with neurological deficits.

Features

- leg pain usually worse than back
- pain often worse when sitting

The table below demonstrates the expected features according to the level of compression:

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Site of compression	Features
L3 nerve root compression	Sensory loss over anterior thigh Weak quadriceps Reduced knee reflex Positive femoral stretch test
L4 nerve root compression	Sensory loss anterior aspect of knee Weak quadriceps Reduced knee reflex Positive femoral stretch test
L5 nerve root compression	Sensory loss dorsum of foot Weakness in foot and big toe dorsiflexion Reflexes intact Positive sciatic nerve stretch test
S1 nerve root compression	Sensory loss posterolateral aspect of leg and lateral aspect of foot Weakness in plantar flexion of foot Reduced ankle reflex Positive sciatic nerve stretch test

Management

- similar to that of other musculoskeletal lower back pain: analgesia, physiotherapy, exercises
- if symptoms persist then referral for consideration of MRI is appropriate

Source:

Still's disease in adults

Adult Still's disease

- typically affects 16-35 year olds

Features

- arthralgia
- elevated serum ferritin
- rash: salmon-pink, maculopapular
- pyrexia
- lymphadenopathy
- rheumatoid factor (RF) and anti-nuclear antibody (ANA) negative

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Pseudoxanthoma elasticum

Pseudoxanthoma elasticum is an inherited condition (usually autosomal recessive*) characterised by an abnormality in elastic fibres

Features

- retinal angioid streaks
- 'plucked chicken skin' appearance - small yellow papules on the neck, antecubital fossa and axillae
- cardiac: mitral valve prolapse, increased risk of ischaemic heart disease
- gastrointestinal haemorrhage

*there are reports of autosomal dominant inheritance in a minority of cases

Fibromyalgia

Fibromyalgia is a syndrome characterised by widespread pain throughout the body with tender points at specific anatomical sites. The cause of fibromyalgia is unknown.

Epidemiology

- women are 10 times more likely to be affected
- typically presents between 30-50 years old

Features

- chronic pain: at multiple site, sometimes 'pain all over'
- lethargy
- sleep disturbance, headaches, dizziness are common

Diagnosis is clinical and sometimes refers to the American College of Rheumatology classification criteria which lists 9 pairs of tender points on the body. If a patient is tender in at least 11 of these 18 points it makes a diagnosis of fibromyalgia more likely

The management of fibromyalgia is often difficult and needs to be tailored to the individual patient. A psychosocial and multidisciplinary approach is helpful. Unfortunately there is currently a paucity of evidence and guidelines to guide practice. The following is partly based on consensus guidelines from the European League against Rheumatism (EULAR) published in 2007 and also a BMJ review in 2014.

- explanation
- aerobic exercise: has the strongest evidence base
- cognitive behavioural therapy
- medication: pregabalin, duloxetine, amitriptyline



Methotrexate is an antimetabolite that inhibits dihydrofolate reductase, an enzyme essential for the synthesis of purines and pyrimidines. It is considered an 'important' drug as whilst it can be very effective in controlling disease the side-effects may be potentially life-threatening - careful prescribing and close monitoring is essential.

Indications

- inflammatory arthritis, especially rheumatoid arthritis
- psoriasis
- some chemotherapy acute lymphoblastic leukaemia

Adverse effects

- mucositis
- myelosuppression
- pneumonitis
- pulmonary fibrosis
- liver cirrhosis

Pregnancy

- women should avoid pregnancy for at least 3 months after treatment has stopped
- the BNF also advises that men using methotrexate need to use effective contraception for at least 3 months after treatment

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Define

Prescribing methotrexate

- methotrexate is a drug with a high potential for patient harm. It is therefore important that you are familiar with guidelines relating to its use
- methotrexate is taken weekly, rather than daily
- FBC, U&E and LFTs need to be regularly monitored. The Committee on Safety of Medicines recommend 'FBC and renal and LFTs before starting treatment and repeated weekly until therapy stabilised, thereafter patients should be monitored every 2-3 months'
- folic acid 5mg once weekly should be co-prescribed, taken more than 24 hours after methotrexate dose
- the starting dose of methotrexate is 7.5 mg weekly (source: BNF)
- only one strength of methotrexate tablet should be prescribed (usually 2.5 mg)
- avoid prescribing trimethoprim or cotrimoxazole concurrently - increases risk of marrow aplasia

De Quervain's tenosynovitis

De Quervain's tenosynovitis is a common condition in which the sheath containing the extensor pollicis brevis and abductor pollicis longus tendons is inflamed. It typically affects females aged 30 - 50 years old

Features

- pain on the radial side of the wrist
- tenderness over the radial styloid process
- abduction of the thumb against resistance is painful
- Finkelstein's test: with the thumb is flexed across the palm of the hand, pain is reproduced by movement of the wrist into flexion and ulnar deviation

Management

- analgesia
- steroid injection
- immobilisation with a thumb splint (spica) may be effective
- surgical treatment is sometimes required

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